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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/27/01; 060	05/19/00	MAVUNKEL	B 21900-20290.

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HM22/0910

EXAMINER

CHANG, C

ART UNIT

PAPER NUMBER

1625

DATE MAILED:

09/10/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

## Office Action Summary

Application No.

09/575,060

Applicant(s)

MAVUNKEL ET AL.

Examiner

Celia Chang

Art Unit

1625

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☐ Responsive to communication(s) filed on 22 June 2001.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☐ Claim(s) 1-9, 11, 12 and 14-42 is/are pending in the application.  
4a) Of the above claim(s) 14 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☐ Claim(s) 1-9, 11, 12, 15-21, 29-33, 36-42 is/are rejected.
- 7) ☐ Claim(s) 22-28, 34 and 35 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

### Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).  
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

### Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s) \_\_\_\_\_
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_ 6) ☐ Other: \_\_\_\_\_

**DETAILED ACTION**

1. Election and amendment filed by applicants in Paper No. 7, dated Jun 22, 2001 have been entered. Claims 10, 13, 43, 44 have been canceled. Claims 1-9, 11-12, 15-42 reading on the elected compounds of group I with compound No. 135 as the elected species, are prosecuted. Claim 14 is withdrawn from consideration as being drawn to the non-elected invention per 37 CFR 1.142(b).

2. Claim 8, 30 and 38 are rejected as being of improper dependent format since the claims recite the limitation of "R<sup>7</sup>", "H<sup>1</sup>" or the limitation of "compounds shown in Table 2 and 3". There is insufficient antecedent basis for the limitation R<sup>7</sup> or H<sup>1</sup> since no definition of these variables were found in the base claim. It is improper to incorporate description in claim 38 because claims must stand alone to define invention and incorporation into claims by express reference to specification is not permitted. *Ex parte Fressola* 27 USPQ2d 1608.

3. Claim 42 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Please note that the term "mediated" encompassed enhancement as well as inhibitory processes which can not be operating simultaneously. Therefore, it is unclear "what" conditions are being treated in the claim.

4. Claim 42 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for employing the compounds as p38- $\alpha$  inhibitors, does not reasonably provide enablement for all p38- $\alpha$  enzyme activity such as encompassed by the claim. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to operate the invention commensurate in scope with the claim.

Claim 1 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making and using compounds wherein the L1 and L2 moieties as described on page 7 or W and X described on page 10, does not reasonably provide enablement for compounds of the claim wherein the L1 and L2 resulted in distance between Ar and  $\alpha$ -ring being

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4.5-24 Å and W and X are 2-6 Å. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make such compounds commensurate with the scope of the claim. Please note that many linking structure can meet the length requirement but only those described on pages 7 and 10 find support of antecedent basis and operable chemical bonding/synthesis guidance. While length can define the size of a molecule, size of a chemical compound without bonding limitation does not meet the enablement requirement for patentability because starting material sources and their reasonable success in chemical synthesis must be considered. In re Howarth 210 USPQ 689.

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-9, 11-12, 15-21, 29, 31-33, 36-37, 39-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Takashima JP 09124631 in view of Patani.

Determination of the scope and content of the prior art (MPEP §2141.01)

Takashima generically disclosed applicant's compound for treating heart failure (see p.2 section 0008 heart failure and p.3 formula I, lines 9-10 substituted amino C<sub>1-6</sub> alky). An example is found as delineated by RN 190775-61-2 wherein the substituent corresponding to the WiCOXjY moiety is CH<sub>2</sub>NHNHCOCH<sub>3</sub> while the instant claims is CONHNHCOCH<sub>3</sub> (i=0, Xj=NHNH, i.e. a 2-6 Å linker, Y is COR<sub>2</sub> and R<sub>2</sub>=CH<sub>3</sub>, i.e. noninterfering).

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

Takashima disclosed all the elements of the claims except the linker has a methylene chain instead of a carbonyl group. Patani taught that the CH<sub>2</sub>NH and the CONH linkers are bioisosteric equivalency (see p.3170, table 48 2<sup>nd</sup> and 6<sup>th</sup> items).

Finding of prima facie obviousness—rational and motivation (MPEP §2142-2143)

Ordinary skill person in the pharmaceutical art is deemed to be aware of all the pertinent art in the field. The above references place the compounds and bioisosteric modification for more similarly active compounds in the possession of artisan in the field. One having ordinary skill would be motivated to employ a bioisosteric modification as disclosed by Patani for the known compound since such bioisosteric equivalency would be expected to have similar activity.

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6. Claims 22-28, 34-35, are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. The compounds of the dependent claims with R3, R4 being nonhydrogen or Z2 being nitrogen are neither anticipated nor rendered obvious by the art of record.


7. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celia Chang whose telephone number is 703-308-4702. The examiner can normally be reached on Monday through Thursday from 8:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner can be reached by facsimile at (703) 308-7922 with courtesy voice message supra.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

CCPC/Chang  
Sept. 6, 2001

  
CEILA CHANG  
PRIMARY EXAMINER  
GROUP 1200 1625